REMARKS

Claims 4, 5, 8 and 12-15 are pending in the application. Claims 4, 5, 8 and 12-15 have been rejected.

Claims 4, 5 and 8 and 12-15 have been rejected under 35 U.S.C. §112, first paragraph. The Examiner contends that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

In particular, the Examiner states:

> It is the Examiner's position that, as Applicant has disclosed only one embodiment of the antibody of the claims, using only said single embodiment, Applicant cannot accurately estimate the size of the antibody genus of which said antibody is a species. Additionally, chimeric antibodies consist of more than just a collection of amino acid fragments, i.e., CDRs. Antibodies comprise complex three dimensional structures in which the CDRs must fit in precise three dimensional space to create an antibody specific for any particular ligand. It is well-known in the immunological arts that the substituting of CDRs into a random framework is highly unlikely to result in an antibody of the same specificity as that of the antibody from which the CDRs were derived. Chimeric antibodies are actually constructed by trial and error starting with a framework that appears to resemble that from which the CDRs were derived. Accordingly a written description that consists only of the CDR regions (and in the case of Claims 4, 5, 8, 14 and 15, just half of the CDR regions) is inadequate to describe the CD25 binding molecule of the instant claims.

Applicants respectfully disagree with the Examiner's conclusion and submit that the specification contains sufficient written description of a CD25 binding molecule as set forth in amended independent Claim 4.

Applicants reiterate the arguments proffered in the previous response to address this rejection.

It is further noted as set forth in the MPEP §2163 (I) that to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. MPEP §2163 (II)(A)(3)(a)(i) further states that whether the specification shows that application was in possession of the claimed invention is not a single, simple determination, but instead is a factual determination reached by considering a number of factors such as level of skill and knowledge in the art, partial structure, and method of making the claimed invention.

Applicants assert that while one specific embodiment of the CD25 binding molecule recited in the claims is disclosed in the present application as argued by the Examiner, such an embodiment coupled with the level of skill in the art, knowledge in the art and a method of making the claimed antigen binding molecule would lead one skilled in the art to recognize that applicant was in possession of the presently claimed method.

The CD25 binding molecule recited in the presently claimed method is described by CDRs having specific sequences. These CDR sequences in defining the antigen binding site

are the relevant identifying characteristics of the recited antibody. The CD25 binding molecule possessing these specific CDR sequences can take on different forms. The CD25 binding molecule can be a chimeric CD25 antibody, wherein the complete variable domains of one antibody are linked to constant domains derived from another antibody. In an embodiment described in the present specification, the complete variable domains are from a mouse Mab and the constant domains are from a human immunoglobulin. A method of producing a CD25 binding molecule having the specified CDR sequences is described in EP 449,769, which is incorporated by reference into the present specification.

The CD25 binding molecule having the specified CDRs can also be a humanized antibody. Typically, the humanized antibody refers to an antibody having an antigen binding site derived from an immunoglobulin from a non-human species, and remaining immunoglobuliin-derived parts of the antibody being derived from a human immunoglobulin. The antigen binding site typically comprises CDR which determine the binding specificity of the antibody molecule and which are carried on appropriate framework regions in the variable domains.

As indicated by the Examiner it is well-known in the immunological arts that the substituting of CDRs into a random framework is highly unlikely to result in an antibody of the same specificity as that of the antibody from which the CDRs were derived. At the time of filing of the present application, however, a number of successful methods for making humanized antibodies were well-known in the art. These methods, rather than substituting CDRs into a random framework, involve the selection of specific amino acids for the framework region to maximize binding of the humanized antibody to the antigen. For example, the specified CDRs from a murine antibody can be grafted into the DNA coding for the framework of a human antibody as described, e.g., in EP-A-0239400 (Winter). Another example of a method for selecting specific amino acids for the framework region to improve binding affinity of the humanized antibody is described in detail, e.g., in U.S. Patent 6,180,370 (Queen). Various methods for producing humanized antibodies having improved binding affinity that were state of the art at the time of filing of the present application are also summarized, e.g., in Vaswani et al., "Humanized antibodies as potential therapeutic drugs" Ann. Allergy Asthma Immunol. 81: 105-119, 1998, a copy of which is attached (see pages 106-108). Accordingly, rather than the method of producing framework regions being a random, trial and error approach as stated by the Examiner, there were well-known methods in the immunological arts at the time of filing of the present application to design humanized antibodies having improved binding affinity by selection of specific amino acids for the framework regions.. Accordingly, a written description of the specific, relevant, CDR regions of the CD25 binding molecule coupled with high skill and knowledge in the art of how to design such humanized antibodies possessing framework regions that can improve antibody affinity and disclosure of how to make the CD25 antibody recited in the presently claimed method would lead one skilled in the art to the conclusion that the applicant was in possession of the claimed invention.

In addition to chimeric and humanized antibodies, techniques for making fragments of the aforementioned antibodies are well known in the art. Thus, one skilled in the art would recognize that in view of the embodiment disclosed in the present application, the high level of skill in the art and knowledge in the art on how to make the aforementioned antibodies, there are a representative number of antibodies that are sufficiently described by the specific CD25 antibody recited in independent Claim 4.

In view of the above, withdrawal of the rejection of Claims 4, 5, 8 and 12-15 under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 4, 5 and 8 have been rejected under 35 U.S.C. §103(a) as being unpatentable over WO 89/09622 (WO'622) in view of Kovarik et al. In particular, the Examiner states:

> The reference [WO'622] does teach that "The present invention provides novel compositions useful in the treatment of T-cell mediated human disorders, the compositions containing a chimeric antibody specifically capable of binding to human IL-2 receptors, such as at the epitope bound by the anti-Tac monoclonal antibody. The IL-2 chimeric antibody can have two pairs of light chain/heavy chain complexes, wherein at least one pair has chains comprising mouse variable regions joined with human constant region segments, with or without naturally-associated J and D segments" (page 3) and further teaches rheumatoid arthritis (RA) as one such disease. In other words, the reference teaches the use of a chimeric anti-IL2 receptor antibody for the treatment of RA. Kovarik et al. teaches the chimeric anti-IL2 receptor antibody basiliximab which comprises the CDRs of the instant claims. Accordingly, the combined references need comprise nothing more than the substitution of obvious equivalents for a proper obviousness type rejection. However, the Kovarik et al. reference teaches more. It also teaches that basiliximab can achieve IL2 receptor saturation and that the antibody is well tolerated, thus basiliximab could be considered to be not just an equivalent of the antibody of the '622 document, but a preferred substitution for said antibody....

Applicants respectfully disagree with the Examiner's conclusion and submit that the combination of references does not make obvious Claims 4, 5 and 8 for the reasons below.

Applicants reiterate the arguments proffered in the previous Office Action to address this rejection. In particular, WO'622, while describing anti-TAC chimeric antibodies, does not teach the antibodies recited in independent Claim 4, or that such antibodies can be utilized to treat rheumatoid arthritis.

Kovarik et al., while teaching the specific chimeric monoclonal antibody, basiliximab, and the use of this antibody for immunoprophylaxis against acute rejection in renal transplantation fail to specifically suggest that binding of basiliximab to IL-2 receptor at serum concentrations sufficient to saturate the receptor to treat transplant rejection would also be effective to treat rheumatoid arthritis.

Accordingly, there is nothing in the combination of references that specifically suggests that basiliximab can be effectively utilized to treat rheumatoid arthritis.

The Examiner alleges that the basiliximab antibody described in Kovarik et al. can be considered a preferred substitute for the anti-TAC antibody described in WO'622 because basiliximab can achieve IL2 receptor saturation and is well tolerated. Thus, it is the Examiner's position that one skilled in the art would be motivated to substitute the anti-Tac antibody with basiliximab to treat rheumatoid arthritis making the presently claimed subject matter obvious.

It would appear that the Examiner's conclusion of obviousness appears to suggest that he is applying an "obvious to try" standard which has consistently been proscribed by the Federal Court. Note the Federal Court's instruction in *The Gillette Co. v. S.C. Johnson & Johnson Inc.*, 16 U.S.P.Q.2d. 1923, 1928 (Fed. Cir. 1990). *In re Eli Lilly & Co.,* 902 F.2d 943, 945, 14 U.S.P.Q.2d. 1741, 1743 (Fed. Cir. 1990), wherein the Court noted:

As we recently explained,

> [a]n "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued. *The Gillette Co. v. S.C. Johnson & Johnson Inc.*, 16 USPQ2d 1923, 1928 (Fed. Cir. 1990). *In re Eli Lilly & Co.,* 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990).

Thus, while WO'622 and Kovarik et al. might arguably pique one's interest in pursuing studies to determine the effect of basiliximab in treating rheumatoid arthritis, there is no teaching in any of the references specifically suggesting how to obtain this desired result or that such a result would be obtained if certain direction were pursued. Accordingly, there is insufficient information in the cited art of record which would lead one skilled in the art to the present invention. Consequently, to suggest that the presently claimed method is obvious is nothing more than an **invitation to experiment** which is not allowed.

In view of the above, withdrawal of the rejection of Claims 4, 5 and 8 under 35 U.S.C. §103(a) is respectfully requested.

A good faith effort has been made to place the present application in condition for allowance.

If the Examiner believes that a telephone conference would be of value, he is requested to call the undersigned counsel at the number listed below.

Respectfully submitted,

Susan Hess

Novartis
Corporate Intellectual Property
One Health Plaza, Building 430
East Hanover, NJ 07936-1080
(862) 778-7859

Susan Hess
Attorney for Applicants
Reg. No. 37,350

Date: October 28, 2003